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Serum IgD and IgE in Rheumatoid Arthritis

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Abstract

Serum immunoglobulins IgD and IgE have been determined by a single radial immunodiffusion technique and a radioimmunoassay method in serum samples from 95 rheumatoid patients, 5 subjects with Sjögren's syndrome and 50 healthy controls, and compared with levels of IgG, IgM and IgA fractions measured in the same subjects. The IgD and IgE serum content resulted similar in the rheumatoid, Sjögren's and control sera. No correlation of IgD and IgE values with changes of other immunoglobulins or with the activity and the duration of the rheumatoid disease was observed.

Introduction

Several authors (6, 23, 33) measured immunoglobulins concentration in patients with rheumatoid arthritis (RA) and found they had significantly higher IgG and IgA serum levels than controls. IgD and IgE constitute classes of human immunoglobulins which are distinct from IgG, IgA and IgM fractions (15, 17, 29). The measurement of IgD and IgE concentrations might contribute to a better knowledge of the role and the involvement of these immunoglobulins in hypersensitivity phenomena and in other immune responses. The purpose of the present investigation was to study the IgD and IgE behaviour in RA in order to ascertain whether noticeable increases of these fractions are observable in this disease, as expression of a polyclonal gammopathy, and the eventual relationship with the activity and the duration of the disease.

Materials and Methods

IgD and IgE serum concentrations were determined in 50 volunteer control subjects without signs of illness, in 5 subjects with Sjögren's syndrome and in 95 patients with definite or classical RA, clinically and radiologically ascertained according to the ARA criteria, with a positivity for latex-test varying from 1 : 40 to 1 : 2560 and for Waaler-Rose from 1 : 32 -1 : 2048. The control group was age matched with study group. For comparison, also serum levels of IgG, IgA and IgM were examined in all subjects. Quantitative estimation of IgD, IgG, IgA and IgM was made by radial diffusion in agar plates (immunodiffusion plates:

Meloy Laboratories, Springfield/Virginia) using the method of Mancini and others (22). The diameters of the precipitin rings were measured after 24 hours of incubation at room temperature and were recorded as blindtest. A series of dilutions standard was used to calibrate every plate. Serum IgE levels were measured by a radioimmunosorbent test (Phadebas IgE test, Pharmacia Laboratories) utilizing anti-IgE antibodies covalently bound to Sephadex particles as a solid phase reactant. This test is relatively simple and is accurate to IgE concentrations as low as 10 ng/ml. IgG, IgA and IgM levels were expressed as mg/ml. IgD values as mg per 100 ml, while IgE concentrations were expressed as ng/ml.

The presence of rheumatoid factor (RF) was investigated in all sera by the latex-agglutination slide test (Hyland Laboratories, Los Angeles/California) and by Waaler-Rose technique modified according to Valkenburg (32).

Results

The quantitative results are shown in Table 1 and 2. In patients with RA the mean level of IgG, IgA and IgM resulted respectively of 16.33 ± 5.70, 3.70 ± 2.20, and 1.24 ± 0.70 mg/ml in comparison to values of 16.50 ± 6.20, 3.58 ± 1.80, and 1.18 ± 0.90 obtained in Sjögren's patients and of 12.15 ± 2.36, 2.87 ± 1.10, and 1.20 ± 0.85 mg/ml observed

Tab. 1. IgG-, IgA-, IgM-immunoglobulin concentrations

Ig type	Serum sample	Mean immunoglobulin concentration ± S.D. (mg/ml)
IgG	Normal subjects	12.15 ± 2.36
	Sjögren's syndrome	16.50 ± 6.20
	Rheumatoid patients	16.33 ± 5.70
IgA	Normal subjects	2.87 ± 1.10
	Sjögren's syndrome	3.58 ± 1.80
	Rheumatoid patients	3.70 ± 2.20
IgM	Normal subjects	1.20 ± 0.85
	Sjögren's syndrome	1.18 ± 0.90
	Rheumatoid patients	1.24 ± 0.70

Tab. 2. IgD- and IgE-immunoglobulin concentrations

Ig type	Serum sample	Mean immunoglobulin concentration ± S.D.
IgD (mg/100 ml)	Normal subjects	5.8 ± 5.5
	Sjögren's syndrome	4.8 ± 3.6
	Rheumatoid patients	5.5 ± 4.2
IgE (ng/ml)	Normal subjects	250 ± 110
	Sjögren's syndrome	210 ± 95
	Rheumatoid patients	280 ± 150

in the group of control subjects. This finding confirms the previously reported data (23). IgD and IgE levels of rheumatoid and Sjögren's sera did not differ significantly from those of control subjects. The mean serum IgD of rheumatoid patients was 5.5 ± 4.2 mg/100 ml, compared to the Sjögren's patients mean of 4.8 ± 3.6 and to the healthy controls mean of 5.8 ± 5.5 mg/100 ml. The mean concentration of IgE resulted of 250 ± 110 ng/ml in the group of controls, 210 ± 95 ng/ml in Sjögren's patients and 280 ± 150 ng/ml in subjects with RA. These differences are not statistically significant.

Discussion

The results obtained suggest that normal concentrations of IgD and IgE may occur in RA in association with increased amount of other immunoglobulin classes. No correlation of IgD and IgE values with those of the other immunoglobulins or with the activity and the duration of the disease was observed. This finding suggests that IgD and IgE regulation appears unrelated to that for IgG, IgA and IgM. Our results confirmed the data obtained by Rowe et al. (28) and Onodera et al. (25) who did not observe any modification of serum IgD in a group of subjects with rheumatoid arthritis or systemic lupus erythematosus (SLE).

The normal serum concentration of IgD and IgE in rheumatoid patients as compared to the other immunoglobulin changes remains to be explained at the present. During the past years a number of studies have been concerned with the class of immunoglobulins IgD. However, there has been little indication on the biological significance and antibody activities of these fractions compared with those of other immunoglobulins (11, 19). It has been suggested that IgD either are seldom involved in immune responses or have such a low affinity for specific antigens that antibody activity is difficult to detect (11). However, some authors found IgD antinuclear antibodies in patients with SLE (18, 27) and IgD antibodies to insulin in some diabetic patients (7), and some others observed subjects which developed IgD antibodies to milk proteins, bovine serum albumin and gamma globulin and diphtheria toxoid (11). IgD levels were not increased in some autoimmune diseases (19), but increased levels were noted in the sera from individuals with high titers of reaginic antibodies (19) and in some patients having chronic infections (28). On the contrary, it is now well known that IgE are carriers of the reaginic antibody activity (14, 15, 17). Serum concentrations of IgE were found to be significantly elevated in patients with allergic diseases (3, 8, 9, 12, 16, 21, 30, 31), but also in pathological conditions other than classical allergy (liver cirrhosis, myeloma, chronic or recurrent infections, coeliac disease) (2, 5, 10). Many factors other than the atopic state seem to be important in de-

termining serum IgE concentration, as the seasonal pollen exposure, the immunotherapy and the severity of the associated atopic disease (20). On the other hand, a significant decrease in serum IgE levels occurred with long term corticosteroid therapy (4, 20).

The nature of the factors involved in determining immunoglobulins levels is not known. Serum immunoglobulins levels represent the equilibrium between catabolism and synthesis in normal conditions, and the amount of immunoglobulins may be related to many factors, such as the environment, the genetic regulation of protein synthesis and metabolism and the antigenic stimuli (24). Particularly, some authors have stressed that the nature of the antigenic stimulation may be an important factor in determining the type of response of each immunoglobulin fraction (13). On the other hand, the absence of a parallel increase for each single component is a common finding in the group of diseases in which an increase of immunoglobulins was observed (13). Furthermore, a statistical analysis demonstrated that the amount of one class of immunoglobulin present in an individual is largely unrelated to the concentration of the other classes (1). We did not observe abnormal serum concentrations of IgD and IgE in our rheumatoid patients, neither any correlation between IgD and IgE levels and the severity of clinical symptoms. This fact and the observation that rheumatoid factors of IgM, IgG and IgA class have been well documentated in RA (26) on one hand, while no evidence was obtained up to the present time on the existence of rheumatoid factors of IgD or IgE class on the other hand, suggest that the role and the importance of IgD and IgE immunoglobulins may be excluded or considered to be negligible in hypersensitivity phenomena and in immunological response related to rheumatoid arthritis.

Zusammenfassung

Serum-IgD- und -IgE-Immunglobuline bei primär chronischer Polyarthritis

Die Serum-IgD- und -IgE-Immunglobuline wurden bei 95 Patienten mit primär chronischer Polyarthritis, bei 5 Personen mit Sjögren-Syndrom und bei 50 gesunden Kontrollpersonen mit Hilfe einer einfachen radialen Immundiffusionstechnik sowie einer Radioimmunassay-Methode bestimmt und mit den IgG-, IgM- und IgA-Spiegeln dieser Versuchspersonen verglichen.

Bei allen 3 Versuchsgruppen ergaben sich ähnliche Werte bezüglich des Serumgehaltes an IgD- und IgE-Immunglobulinen. Eine Korrelation der IgD und IgE-Werte mit Veränderungen anderer Immunglobulinspiegel oder mit Aktivität und Dauer der rheumatischen Erkrankung wurde nicht beobachtet.

Résumé

L'IgD et l'IgE sériques dans la polyarthrite rhumatoïde

Les immunoglobulines sériques IgD et IgE ont été déterminées par technique d'immunodiffusion radiale simple et par méthode radio-immunologique dans des

échantillons de sérums provenant de 95 malades ayant une polyarthrite rhumatoïde, de 5 sujets porteurs d'une syndrome de Sjögren et de 50 sujets témoins en bonne santé, et on les a comparées avec les taux d'IgG, d'IgM et d'IgA mesurés chez ces mêmes sujets. La teneur du sérum en IgD et en IgE a été comparable dans les cas de polyarthrite, du syndrome de Sjögren et chez les témoins. On n'a pas observé de corrélation entre les valeurs d'IgD et d'IgE et les modifications des autres immunoglobulines ou bien l'évolutivité ou la durée de la maladie rhumatoïde.

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